

Profile of HIV Associated Cardiomyopathy and Cardiac Isoform of Alpha Two Macroglobulin

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Citation

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Abstract

The association between dilated cardiomyopathy and HIV is well established. Reports from our lab have shown that Cardiac isoform of alpha two macroglobulin (CA2M) can be used as a marker of cardiac involvement. The present study is to find out the socio demographic and clinical profile of dilated cardiomyopathy in HIV patients and association with CA2M levels. 284 HIV patients with symptoms suggestive of cardiac involvement and 10 controls were included in the study. 6.69 percentages were found to have dilated cardiomyopathy (DCM). The mean age was 33.63 ± 6.05 years. The CA2M values were significantly higher in DCM compared to patients without cardiac involvement. Age, sex, duration, socioeconomic status, ejection fraction and CD4 count does not found have any correlation with CA2M levels.

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INTRODUCTION

Involvement of cardiovascular system, either direct or indirect in AIDS has been contemplated to be a major factor contributing to significant morbidity and mortality [1]. HIV associated cardiomyopathy is a well documented complication. CD4 count may not be a useful marker of HIV-associated left ventricular dysfunction [2]. The incidence is high and difficult to diagnose in the initial stages both clinically and with investigations [3, 4, 5, 6, 7, 8]. Dilated cardiomyopathy in HIV-infected patients is associated with a poor prognosis [9]. If it is diagnosed early, preventive and therapeutic strategies for progressive left ventricular dysfunction will be useful [10]. We have reported that Cardiac isoform of alpha 2 macroglobulin can be used as a marker to predict cardiac involvement in HIV patients [11]. The socio demographic profile of dilated cardiomyopathy among the Indian population is not well studied. In the current study, we analyses the socio demographic and clinical profile of dilated cardiomyopathy, its association with CA2M and utility of CA2M in predicting the severity of the lesion in terms of ejection fraction.

MATERIALS AND METHODS

The study has been conducted in Madurai medical college and Maurai Kamraj University. 284 HIV patients with symptoms suggestive of cardiac involvement and 10 controls

were included. An informed consent was obtained from all study participants. Patients were selected based on clinical evaluation, HIV status by standard tests, ECG and two dimensional Transthoracic echocardiogram. Exclusion criteria were severe chronic heart failure (New York Heart Association class III/IV) and acute cardiovascular events (within 90 days before inclusion in the study). Further, sera drawn were subjected to estimation of CA2M levels. Young Wistar albino rats were used in the study. CA2M protein from sera of aorta constricted rats was purified and anti-rat CA2M antisera were raised. The immuno-cross reactivity between human serum CA2M and anti rat CA2M antibody was tested by Western blot analysis and quantification of CA2M levels were carried out by sandwich ELISA. Institutions Ethical committees have cleared the animal experiments and human samples used in this study. Results were statistically analyzed using repeated measures of ANOVA.

RESULTS

6.69 percentages were found to have Dilated cardiomyopathy. The mean age was 33.63 ± 6.05 years. The CA2M values were 108.56 ± 16.51 mg/dl, significantly higher compared to normal subjects (36.93 ± 2.95 mg/dl, Fisher F value =182.08, $p < 0.001$) (See Table 1). Mean ejection fraction was 29.47 ± 8.64 percentage. On ECG, left atrial enlargement was documented in 3 patients, left ventricular hypertrophy in 2 patients and ventricular ectopic beats in 4

patients. The mean CD4 count was $78.31 \pm 36.74 /\text{mm}^3$. 63.1 percentages were men. Duration from diagnosis of HIV was 2.36 ± 1.4 years. 78.9 percentages were from lower socio economic status. Age ($p=0.50$), sex ($p=0.53$), duration from diagnosis ($p=0.80$), socioeconomic status ($p=0.35$), EKG changes ($p=0.24$), ejection fraction ($p=0.91$) and CD4 count ($p=0.07$) does not have significant correlation with CA2M levels (See Table 2).

Figure 1

Table 1

Study populations	Age	CA2M**(mg/dl)
Dilated cardiomyopathy (n=19)	$33.63 \pm 6.05^*$	108.56 ± 16.51
Normal controls (n=10)	32.0 ± 7.14	36.93 ± 2.95

* The values are expressed as Mean \pm standard deviation.

** Cardiac alpha two macroglobulin

Figure 2

Table 2

Patient demographics	Mean \pm SD
Age	33.63 ± 6.05 years
Sex	63.1% men
CD4	$78.31 \pm 36.74 /\text{mm}^3$
EF	29.47 ± 8.64 %
EKG changes	47.3%
Socio economic status	78.9% in lower
Duration from diagnosis	2.36 ± 1.4 years

* The values are expressed as Mean \pm standard deviation.

DISCUSSION

The incidence of dilated cardiomyopathy in Indian population with cardiac symptoms was found to be high. Postulated mechanisms for HIV mediated cardiomyopathy include direct cardiotoxicity of HIV virus, opportunistic infections, autoimmune response, nutritional deficiencies, coinfection with other cardiotropic viruses, post viral cardiac autoimmunity, autonomic dysfunction, and cardiotoxicity

from illicit drugs and pharmacologic agents [12,13,14,15,16]. Though exact mechanism remains elusive, majority consider it to be result of postmyocarditis cardiomyopathy. Idiopathic lymphocytic myocarditis is a common postmortem finding in patients with ventricular dysfunction. The over expression of cytokines TNF- α , IL-6 and inducible nitric oxide synthase evident in endomyocardial biopsies appears to be equally responsible.

CA2M values were high in all patients with HIV associated cardiomyopathy and are found to be independent of other patient parameters. CA2M is not a specific marker for dilated cardiomyopathy. It is likely to be a marker of myocardial injury [17]. The current study shows that it is a reliable marker in HIV associated cardiomyopathy. Ejection fraction was not correlated with CA2M levels. It makes CA2M a poor predictor of the severity of the lesion. ECG changes were observed only in 47.3 percentages of patients. Since the study is conducted in a Government medical college, most of the patients were from poor socio economic strata. The duration between the diagnosis of HIV and cardiac involvement was within 5 years in majority of the patients. It is likely because of the lack of awareness for HIV testing in asymptomatic individuals.

The high prevalence of HIV related dilated cardiomyopathy shows the importance of careful cardiac evaluation from the diagnosis. It is noteworthy that, patients with CD4 counts less than $200 /\text{mm}^3$, within first 5 years of diagnosis, ECG evidence of cardiac involvement will be benefited with CA2M analysis. The usefulness of CA2M is likely to be in the outpatient evaluation in HIV patients prior to extensive work up. Further large scale studies are required to confirm the utility of CA2M in asymptomatic patients.

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